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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,023	01/09/2007	Rene Bernards	BJS-620-445	9239
23117 7590 06/23/2010 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203				
EXAMINER				
CHONG, KIMBERLY				
ART UNIT		PAPER NUMBER		
1635				
MAIL DATE		DELIVERY MODE		
06/23/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/587,023

**Applicant(s)**

BERNARDS ET AL.

**Examiner**

KIMBERLY CHONG

**Art Unit**

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 June 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 and 12 is/are pending in the application.
- 4a) Of the above claim(s) 5-8 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

Applicant's response filed 06/04/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 01/05/2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 06/04/2010 and 02/11/2010, claims 1-8 and 12 are pending in the application. Claims 1-4 are currently under examination.

### ***Response to Applicant's Arguments***

#### ***Claim Rejections - 35 USC § 112***

The rejection of claims 1-4 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record.

Applicant's arguments filed 06/04/2010 have been fully considered but they are not persuasive. Applicant submits the claims should not be narrowed to the preferred embodiments unless the specification suggested the inventor intended such a narrow coverage. Applicant argues that the scope of enablement is not limited to what has been disclosed, it is what is described in the specification plus what is known in the prior art and at the time of the invention, a skilled artisan would be able to practice the exemplified embodiments with some routine experimentation which is not undue

experimentation. Lastly, Applicants argue that the described in vitro and in vivo results are predictive for human therapy because usefulness in a patent invention necessarily includes the expectation of further research and development.

The claims amendments adding new classes of HDAC inhibitors is acknowledged and therefore the scope of enablement rejection with respect to the lack of enablement for the broad genus of inhibitors previously claimed has been withdrawn.

With respect to the lack of enablement for a method of treating the tumors types listed in claim 1, the arguments are not persuasive. The claims are now drawn to treating melanoma, acute leukemia, chronic leukemia, non-small-cell lung carcinoma, head cancer, neck cancer, renal carcinoma and breast cancer. As stated previously, the specification does provide guidance for a method of decreasing A375 melanoma cell proliferation in vitro using a siRNA targeted to a gene encoding PRAME wherein the cells were cultured with a HDAC inhibitor. However, there is no guidance in the specification that would be considered enabling for the breadth of the claimed subject matter and the working embodiment not predictive of the invention as claimed.

Moreover, the prior art is not predictive of methods of treating said tumors using a siRNA inhibitor of PRAME and an inhibitor of HDAC. Tajeddine (Cancer Res 2005) found that overexpression of PRAME in cultured leukemic cells were responsible for a slower proliferation rate of said cells and demonstrates that nude mice injected with siRNA PRAME leukemic cells grew tumors significantly faster than cells that did not have PRAME down-regulated. Thus, at the time of filing, down-regulating of PRAME using siRNA increased the tumorigenicity of leukemic cells.

In a post-filing reference in 2008 by Doolan et al. states that prior to said reference, the prognostic and prevalence of PRAME expression in breast cancer had not yet been investigated. Doolan et al. did find that PRAME expression correlates with an unfavorable outcome of the disease. Doolan et al. do not provide any evidence of methods of treatment of PRAME such that a decrease of expression of PRAME along with treatment of an HDAC inhibitor provided treatments for breast cancer let alone any other type of cancer.

Thus this reference at the time of filing does not provide guidance when coupled with the instant specification that would allow the skilled artisan to practice the full scope of the claimed invention in all the tumor types recited. The instant specification does not provide a correlation between treatment effects in a melanoma cell with treatment effects in a leukemic or breast cell for example such that the skilled artisan would know that inhibition of PRAME expression would cause apoptosis in the claimed tumor types just as demonstrated in melanoma cells. Without this correlation or guidance in the specification on treating any of the tumor types claimed and given it has been shown in the art that PRAME inhibition appears to have the apposite effect of increasing tumorigenicity in some cancers as that which is instantly claimed, the skilled artisan would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Thus the rejection is maintained.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Fereydoun Sajjadi at 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/  
Primary Examiner  
Art Unit 1635